

CLAIMS

1. A method used, during the solid-state synthesis of surface-bound polymers on a solid substrate, for removing a reaction solution including unreacted reactive reagents from the surface of the solid substrate and from any nascent polymers bound to the solid substrate, the method comprising:

selecting a reactive wash solution that is not reactive toward, and does not catalyze reactions with, the solid substrate or any nascent polymers bound to the solid substrate but that reacts with, and deactivates, the reactive reagents and that is miscible with the reaction solution; and

applying the reactive wash solution to the surface of the solid substrate in order to react with, and deactivate, any unreacted reactive reagents and to remove the reaction solution from the surface of the solid substrate and from any nascent polymers bound to the substrate.

2. The method of claim 1 wherein the reaction solution includes reactive monomers and a catalyzing reagent that catalyzes the coupling of reactive monomers to the nascent polymers.

3. The method of claim 2 wherein the reactive monomers are deoxynucleoside phosphoramidites and the polymers are oligonucleotides.

4. The method of claim 3 wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized, the method further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidites; and

rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated unreacted deoxynucleoside phosphoramidites and catalyzing reagent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

5. The method of claim 3 wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized, the method further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidite s;

allowing the applied reactive wash solution and reaction solution to evaporate; and

rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated deoxynucleoside phosphoramidite s and catalyzing agent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

6. The method of claim 3 wherein the reactive wash solution includes a chemical compound containing a hydroxyl functional group.

7. The method of claim 6 wherein the reactive wash solution is methanol.

8. The method of claim 1 wherein the reaction solution includes a reactive dye.

9. The method of claim 1 wherein the reaction solution includes a reactive radio-labeled marker.

10. A method for coupling a reactive monomer molecule to a nascent polymer bound to surface of a solid substrate, the method comprising:

applying monomer molecules and any reagents required to catalyze the coupling of the reactive monomer molecule with the nascent polymer to the surface of the solid substrate; and

applying a reactive wash solution to the surface of the solid substrate to react with, and deactivate, any remaining reactive monomers on the surface of the solid substrate and to dissolve and remove the remaining deactivated monomers and any reagents required to

catalyze the coupling of the reactive monomer molecule to the polymer from the surface of the solid substrate and from any synthesized polymers bound to the substrate.

11. The method of claim 10 wherein the reactive monomers are deoxynucleoside phosphoramidite s and the polymers are oligonucleotides.

12. The method of claim 11 wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized, the method further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidite s; and

rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated unreacted deoxynucleoside phosphoramidite s and catalyzing reagent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

13. The method of claim 12 wherein the solid substrate is a high-density array comprising cells in which different oligonucleotides are synthesized, the method further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidite s;

allowing the applied reactive wash solution and solution to evaporate; and

rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated deoxynucleoside phosphoramidite s and catalyzing agent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

14. The method of claim 11 wherein the reactive wash solution includes a chemical compound containing a hydroxyl functional group.

15. The method of claim 14 wherein the reactive wash solution is methanol.

16. A high-density array comprising cells containing different polymer species bound to the surface of the high-density array and synthesized on the surface of the high-density array by the step-wise coupling of reactive monomers to nascent polymers bound to the surface of the high-density array, the step-wise coupling of reactive monomers to nascent polymers comprising the steps of:

applying reactive monomer molecules and any reagents required to catalyze the coupling of the reactive monomer molecule to the nascent polymer to the surface of the solid substrate; and applying a reactive wash solution to the surface of the solid substrate to react with, and deactivate, any remaining reactive monomers on the surface of the solid substrate and to dissolve and remove the remaining deactivated monomers and any reagents required to catalyze the coupling of the reactive monomer molecule with the polymer from the surface of the solid substrate and from any synthesized polymers bound to the substrate.

17. The high-density array of claim 17 wherein the reactive monomers are deoxynucleoside phosphoramidite s and the polymers are oligonucleotides.

18. The method of claim 17 further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidite s; and rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated unreacted deoxynucleoside phosphoramidite s and catalyzing reagent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

19. The method of claim 17 further including:

applying the reactive wash solution separately to each cell of the high-density array in order to react with, and deactivate, any unreacted deoxynucleoside phosphoramidite s; allowing the applied reactive wash solution and solution to evaporate; and

rinsing the surface of the solid substrate with the reactive wash solution to remove the deactivated deoxynucleoside phosphoramidite s and catalyzing agent from the surface of the solid substrate and from any nascent polymers bound to the substrate.

20. The method of claim 17 wherein the reactive wash reagent is methanol.